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# "ADAPTIVE INFORMATION PROCESSING IN AUDITORY CORTEX"

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## INTRODUCTION

The principles of biological intelligence are of central importance to the understanding of brain function and to the development of devices based on the extraordinary computing and information processing abilities of brains. Adaptive cognitive and behavioral performance must be based on principles of brain function that have been selected in evolution so that organisms can successfully cope with environmental demands. Although these principles are not yet known, they may be advantageously approached by analyzing how they modify information processing within the brain. Central to adaptive information processing, as expressed in the mammalian brain, are the cerebral neocortex and associative learning. In both fields, new perspectives are emerging. In particular, information processing in sensory neocortex involves the operation of active learning processes which transform receptive fields (Weinberger and Diamond, 1987).

As explained in more detail later, associative learning causes a rapid, non-transient, frequency-specific plastic change in the receptive fields of single neurons in the auditory cortex. The dynamic characteristics of coding imply that the functional organization of information in sensory cortex comprises an adaptively-constituted information base. The foundation of this process appears to be the receptive fields of individual neurons which form filters that are "re-tuned" according to the behavioral significance of stimuli. These and related findings provide a basis for understanding the functional role of sensory cortical physiological plasticity and form a bridge between physiological plasticity and adaptive information processing in the cerebral cortex.

## BACKGROUND

### The Use of Classical Conditioning to Elucidate Adaptive Information Processing

Classical conditioning has proven to be a rich source of theoretical issues and empirical investigations for both behavioral and neurobiological inquiries into the domain of learning and memory. There are two contrasting approaches to the neurophysiological study of learning and memory. "S-R circuit analysis" seeks critical loci of neuroplasticity which underlie the acquisition of particular motor conditioned responses. "Adaptive information processing" focuses on how learning alters neural representations of sensory events, as animals acquire information about their behavioral significance or meaning. Within the neurophysiology of classical conditioning, this approach entails an analysis of the responses of neurons to conditioned stimuli (CS) within the appropriate sensory system.

There is no logical incompatibility between S-R circuit tracing and adaptive information processing. Indeed, to some extent the approaches may appear indistinguishable, as when the former involves recording from the sensory system of the conditioned stimulus. But their goals are quite different. Adaptive information processing has an informational endpoint in the brain, rather than a motor endpoint.

Previously, we have summarized theoretical and empirical arguments that the two approaches emphasize different sequential stages in associative learning (e.g., Weinberger and Diamond, 1987). Our analyses support Konorski's (1967) hypothesis that two types of conditioned responses develop within all training situations. Our recent survey of conditioning studies (Lennartz and Weinberger, in preparation) revealed that there is a basic dichotomy in learning rates for response systems employed in classical conditioning: autonomic conditioned responses develop rapidly,

(5-10 trials), whereas nictitating membrane, eyelid retraction, and limb or tail flexion require 60-90 trials (Weinberger, 1982a,1984; Weinberger, Diamond and McKenna, 1984; Weinberger and Diamond, 1987).

This behavioral dichotomy is consistent with the view that classical conditioning involves (1) a rapidly-developing stage in which animals learn that the conditioned stimulus predicts the unconditioned stimulus, this is detected behaviorally as the rapid, simultaneous development of autonomic conditioned responses and (2) a slowly-developing stage in which animals learn to make a single somatic conditioned response which is specific to the type and location of the unconditioned stimulus, e.g., eyeblink for air puff to the eye or flexion for shock to a limb. That S-S precedes by S-R learning is consonant with the fact that classical conditioning involves higher functions as well as response learning. Because S-S learning (about the CS-UCS relationship) is acquired very rapidly, it could be required for the slower, specific response learning.

Because the first events in learning appear to be the acquisition of information (rather than the acquisition of specific motor responses), we have attacked the foundational problem of how information is acquired, that is, how the brain accomplishes adaptive information processing. We have used the auditory system because of extensive documentation that learning alters the responses of this system to acoustic stimuli (Weinberger, 1984; Weinberger, Diamond, and McKenna, 1984; Weinberger and Diamond, 1987).

## PREVIOUS FINDINGS

Here we briefly summarize those of our previous findings that are most relevant to the current research contract.

### Plasticity in the Auditory Thalamus

Previously, we discovered that learning involves differential plasticity at the thalamic level of the auditory system of the cat. The lemniscal ventral medial geniculate nucleus (MGv) is not plastic. In contrast, discharge plasticity develops rapidly in the magnocellular medial geniculate (MGm) (Ryugo & Weinberger, 1978; Weinberger, 1982a). In brief, the MGv provides the cortex with precise information about the physical parameters of sound, and this information is not subject to modification. On the other hand, the MGm provides the auditory cortex with precise information about the importance of sound, e.g., the extent to which it signals an aversive stimulus. This information is modified to track stimulus significance, e.g., "tone signals aversive reinforcement". The site of convergence of information from the auditory and somatosensory-nociceptive system is in the MGm, the synapses of which can develop plasticity, e.g., long-term potentiation (Gerren & Weinberger, 1983; Weinberger, 1982b).

### Plasticity in the Auditory Cortex

At the level of auditory cortex, learning induces a rapidly-developing discharge plasticity at the level of both "clusters" and single neurons. Associatively-induced plasticity in both the MGm and the auditory cortex develops during discrimination learning and exhibits retention for at least one week post training (Oleson, Ashe and Weinberger, 1975; Weinberger, Hopkins, and Diamond, 1984; Diamond & Weinberger, 1984).

The sites of information transformation during learning in the auditory system seem to be confined largely to the MGm-cortex sub-system. Supportive evidence is that the lemniscal input to the cortex is not plastic. Also, the receptor potential (cochlear microphonic) is not plastic (Ashe, Cassady and Weinberger, 1976). Thus, neither peripheral gating nor putative changes in the lower auditory system can account for associatively-induced plasticity in the auditory thalamo-cortex. Finally, direct measures of arousal level (tonic and phasic pupillary size) indicate that the physiological plasticity in auditory thalamo-cortex is associative rather than due to state of arousal (Weinberger and Diamond, 1987; Diamond and Weinberger, 1989).

Adaptive Information Processing: Receptive Field Plasticity in Auditory Cortex

These findings, by themselves, do not directly resolve a critical issue in adaptive information processing. Thus, learning-induced sensory cortical plasticity could reflect either (1) a general change in cortical responsivity or (2) a specific change in the way that information is processed by sensory cortex. Direct tests of these alternatives have been attempted, and it has been claimed that the results support the "general change" hypothesis. Detailed critiques of these claims have been presented elsewhere (Weinberger and Diamond, 1988). For present purposes, it is sufficient to note that those findings are inconclusive due, in part, to the absence of adequate controls for non-associative factors.

In order to resolve this issue, it is insufficient to test learning effects on neuronal responses to a single stimulus, as done in previous studies. Rather, it is necessary to determine the effects of learning on the processing of a stimulus dimension. Under a prior contract, we have combined sensory physiology and learning paradigms within the same experiment to accomplish this task.

Tuning curves were obtained from single neurons before and after each stage of classical conditioning (sensitization, pairing, extinction, retention). It was revealed that physiological plasticity in the secondary (AII) and ventral ectosylvian (VE) auditory fields actually reflects a highly specific change in the frequency receptive fields of single neurons -- the greatest effect is at the frequency of the conditioned stimulus. The receptive fields are stable in the absence of conditioning, and the changes in receptive fields are maintained unless the behavioral learning is altered by extinction, in which case they revert to pre-conditioning status. These effects were found for both narrowly and broadly-tuned cells (Diamond and Weinberger, 1986; Weinberger and Diamond 1988).

These results indicate that the "processing specificity" theory is correct. In other words, the encoding of stimuli whose significance is acquired by experience is accomplished by retuning the receptive fields of single neurons.

The Functional Mosaic: Context-Dependent Expression of Plasticity in Cortex

From a formal standpoint, the tuning curves of neurons have much in common with the filtering properties of man-made information processing networks. An analysis of cortical tuning curves revealed that tuning curves behave as adaptive filters when learning occurs. But the brain differs from man-made devices in fundamental ways. Chief among these is the distinction between the induction and the expression of adaptive filtering. These processes are separately revealed when cortical plasticity established in a given training environment or "context" is detected in a different context. While plasticity is induced by associative neural processes during a designated training experience, the amount and pattern of dis-

charges that index plasticity differs when the CS is presented in another context (Diamond and Weinberger, 1989). Such contextual sensitivity is clearly highly adaptive because, unlike motor-skill learning, informational learning allows organisms to make cognitive and behavioral decesions that are appropriate to the current situation. Thus, it seems unlikely that fixed changes in specific circuits could track context. Rather, each neuron may better be considered as a member of a functional mosaic (see Diamond and Weinberger, 1989). Accordingly, attaining an understanding of adaptive information processing (AIP) as evolved in mammalian sensory neocortex demands a broader conceptual framework than does "skill" or "procedural" conditioning. It also entails more exhaustive experimental designs.

Auditory Cortical Fields of Guinea Pig (Cavia Porcellus)

Under this contract, we have extended studies to a rodent, the guinea pig, in order to determine the generality of auditory information processing across families of mammals, bring findings into closer relation with the main corpus of data in brain and learning, i.e., the rodent, and to enable cost-effective experimentation. Previous workers have indicated that the guinea pig has two primary-like auditory fields. We have verified this organization, as a necessary prelude to the investigation of cortical plasticity fields, using quantitive analysis of neuronal responses in the anesthetized guinea pig.

Frequency Specific Plasticity During Habituation in the Auditory Cortex of Guinea Pig

The extent to which different types of learning invoke adaptive information processing is of major interest. In this study, we explored the extent to which AIP is in evidence in a simple form of non-associative learning, habituation. The subjects were guinea pigs bearing chronically-implanted microelectrodes in primary (tonotopi-

cally-organized) auditory cortex. Following determination of tuning curves, a single tone frequency was repeated several hundred times. Response decrements in both clusters of neurons and single cells extracted from clusters were obtained. Post habituation tuning curves revealed the development of a frequency specific decrement centered on the frequency of the repeated stimulus. Adaptation, refractoriness, fatigue, and other non-learning factors were controlled. Therefore habituation produces a frequency-specific change in tuning rather than a general alteration of neuronal excitability. Experience-dependent retuning of frequency receptive fields is therefore characteristic of even the simplest form of learning, habituation.

The Expression of Frequency-Specific Plasticity Under Anesthesia

One method of delineating AIP is to seek neurophysiological representations of memories at a time when no new learning is possible. Accordingly, waking guinea pigs underwent classical aversive conditioning (tone-shock). Frequency receptive fields were determined in the non-lemniscal magnocellular medial geniculate nucleus before and following fear conditioning, while the subjects were under deep general anesthesia (sodium pentobarbital). Learning produced frequency-specific changes in tuning. The major change was at the frequency of the conditioned stimulus. These findings provides the first evidence that learning produces physiological plasticity that can be "read out" under subsequent anesthesia.

Adaptive Information Processing in Auditory Cortex During Classical Conditioning

In order to determine the effects of associative learning in the primary, tonotopic, auditory cortex, guinea pigs bearing chronically-implanted microelectrodes underwent classical conditioning. Following determination of frequency RF, a frequency within the RF was selected as a CS. Comparison of receptive fields before and after conditioning revealed that classical conditioning induced frequency-specific plasticity in

auditory cortex. Interestingly, when the frequency used as the CS was not the best frequency, then it became the best frequency as a result of conditioning. This was accomplished by a coordinated increase in response to the CS frequency and a decrease in response to the previous best frequency. (Bakin, Condon and Weinberger, 1988). Therefore, learning can produce shifts in tuning so that re-tuning is centered on the important frequency. In short, neurons shift their frequency "preference" to "match" changed significance of environmental stimuli.

## Facilitated Discriminative Avoidance Behavior

In order to explore the behavioral domain of tuning curve changes, we have trained guinea pigs in an instrumental avoidance situation to complement work in classical conditioning. Guinea pigs were trained in a Brogden wheel using two tones and CS durations of 10 sec. We were able to facilitate two-tone discrimination by reducing responding to the CS- using a response-contingent paradigm. Responses during the CS+ produced termination of the stimulus and avoidance of shock. Responses to the CS- produced another CS- (10 sec.) until animals no longer responded during this stimulus. In contrast to a control group (non-contingent), the experimental group exhibited superior discriminative performance.

## Adaptive Information Processing in Auditory Cortex During Instrumental Conditioning

We used the facilitated avoidance paradigm described above to determine whether AIP in auditory cortex develops for instrumental conditioning as well as for habituation and classical conditioning. Frequency receptive fields were obtained before and after successful avoidance training. The CS+ was selected as a frequency, often the best frequency, within the response area of the neuron. The CS- was selected in this initial study as a frequency to which neurons were minimally responsive. As

for habituation and classical conditioning, avoidance conditioning resulted in frequency-specific modification of tuning curves. In particular, if the CS+ was also the best frequency, then the major effect was a facilitation of response to the CS frequency (Bakin, Condon, and Weinberger, 1988). This work is ongoing.

## GOALS OF THIS PROJECT

The fact that learning induces frequency-specific modification of receptive fields in auditory cortex implies that the functional organization of auditory (and probably other sensory) cortex comprises an adaptively-constituted information base. This project initiates the first systematic investigation of adaptive information processing in the cerebral neocortex. A major goal is to determine the circumstances under which adaptive information processing is induced by experience. Additionally, this project also addresses central hypotheses about rules that govern adaptive information processing, at three levels of spatial scale: (a) parallel processing in different auditory fields; (b) modular processing in different cortical lamina within fields; (c) local processing in different neurons within the same locus within lamina. Finally, we are formulating and testing two types of models: (1) a global qualitative model in which the interactions of input systems with intrinsic cortical processes constitute the neural framework for adaptive information processing, and (2) a specific formal mathematical model that concerns the detailed, sequential modification of the receptive fields of pyramidal neurons in the auditory cortex.

## PROGRESS DURING THE SECOND YEAR

### Introduction

Given the empirical advances made during the first year, the second year has emphasized theoretical work. Specifically, we have formulated two testable models: (1) a preliminary model of global scope in which three complementary projection systems converge in auditory cortex to establish receptive field plasticity; (2) a mathematical model of RF plasticity for pyramidal cells in the auditory cortex which fits within the framework of the global model. Empirical studies also have been pursued, emphasizing the thalamic sources of input to the auditory cortex. This project also provided partial support for determining the role of acetylcholine in cortical plasticity. Finally, we initiated a major technical effort to record the discharges of many cortical neurons simultaneously.

### Neural Adaptive Information Processing: A Preliminary Model of Receptive Field Plasticity in Auditory Cortex During Pavlovian Conditioning

During the second year of this project, we have made a major effort to develop a testable model of cortical receptive field plasticity. (Weinberger, Ashe, Metherate, McKenna, Diamond, Bakin, and Cassady, in press; Weinberger, Ashe, Metherate, McKenna, Diamond, and Bakin, in press). This model applies to the primary tonotopic auditory cortical fields and is referred to as the "triplex model".

As reviewed in the previous sections, classical conditioning provides for the acquisition of information about the relationship between conditioned (CS) and unconditioned stimuli (UCS), indexed by the very rapid development of autonomic conditioned responses (CR), followed by the emergence of a specific somatic conditioned response which indexes a CS-CR association. During conditioning with an acoustic

CS, physiological plasticity develops in the auditory cortex during the first stage of CS-UCS association. This plasticity is highly specific to the frequency used as the conditioned stimulus. Plasticity in frequency receptive fields in primary auditory cortex is characterized by increased response to the frequency of the conditioned stimulus and decreased responses to adjacent frequencies. These receptive field alterations are often sufficient to produce a shift in best frequency to that of the frequency used as the conditioned stimulus.

Thalamic auditory system input to auditory cortex involves projections to (i) middle layers from the lemniscal ventral medial geniculate body whose neurons exhibit no physiological plasticity during learning, and (ii) apical dendrites of pyramidal cells in layer I from the non-lemniscal magnocellular medial geniculate (MGm) whose neurons rapidly develop physiological plasticity. Additionally, application of muscarinic agonists or anticholinesterases directly to auditory cortex in the absence of conditioning training can produce shifts in receptive fields similar to those obtained during learning (McKenna, Ashe and Weinberger, in press; Ashe, McKenna and Weinberger, in press). Also, cholinergic effects may be highly specific to the tonal frequency present during cortical application of acetylcholine (Metherate and Weinberger, 1989).

Our preliminary model for "neural adaptive information processing" in the primary auditory cortex is based upon the convergence of three types of subcortical influences upon auditory cortex: (1) auditory lemniscal, (2) auditory non-lemniscal and (3) nucleus basalis of Meynert cholinergic (Figure 1). This "triplex model" specifies modified Hebb rules for the strengthening and weakening of synapses on pyramidal cells that receive lemniscal, highly-specific frequency information from the ventral medial geniculate body. Critical to synaptic modification is the magnocellular

medial geniculate nucleus which is thought to increase the excitability of all pyramidal cells during learning. Synapses that are activated by the presence of the frequency of the conditioned stimulus on excited cells are hypothesized to be strengthened simultaneously with the weakening of non-active frequency-specific synapses on those cells, (Figure 2). Synapses are active on non-excited cells are also weakened. Acetylcholine, thought to be released from the nucleus basalis by increased activation of the magnocellular medial geniculate early in learning (via a link from the amygdala) amplifies the MGm excitatory effect on pyramidal cells by increasing dendritic input resistance. The model makes several testable predictions about receptive field plasticity and including changing the representation of frequency across primary auditory cortex (Figure 3).

We suggest that receptive field plasticity in visual and somatosensory cortices, demonstrated by deprivation or alteration of sensory input, may be produced by mechanisms that underlie receptive field plasticity during learning (Weinberger, Ashe, Metherate, McKenna, Diamond and Bakin, in press). In short, a unified theory of cortical plasticity may emerge from neural mechanisms of adaptive information processing in learning. The model also is intended as a heuristic to promote synthesis of sensory neurophysiology and the neurobiology of learning, both of which seek to understand information processing, but traditionally have taken separate paths. Current and future experiments provide tests of the model.

## A Mathematical Model of Cortical Receptive Field Plasticity During Classical Conditioning

Together with Dr. Jack Sklansky (Department of Electrical Engineering, UCI), a testable mathematical model (the "competing window" model) has been formulated. Support for this modeling of cortical adaptive information processing will be pro-

vided by DARPA.

Our approach is to employ a gradient descent approach which is based on a window training procedure that previously has been devised and successfully tested in trainable machines. Our model of the spectral response of neurons in auditory cortical networks will be tested and refined against neurophysiological findings previously obtained in animals. This approach is advantageous in its adherence to neurobiological data, focus on both single cell processes and cellular interactions within the network, including endogenous and exogenous components of plasticity, and representation of receptive fields in state space with determination of learning trajectories of receptive fields within that space.

The work will progress in three stages that are logically linked from simple to complex: (1) modeling the spectral response of auditory cortical neurons to pure tone frequencies for a base state in which learning and neuronal plasticity cannot develop; (2) modeling the spectral response of neurons for the waking brain in which plasticity can develop; (3) modeling the plasticity of the spectral response of neurons that develops during behavioral learning. This project is unique in modeling learning-induced neo-cortical receptive field plasticity and synthesizes proven technologies from neurobiology and mathematical machine learning in modeling real-time computing in biological neural networks.

A detailed explanation of this model is presented in Appendix A.

## Receptive Field Plasticity in the Dorsal Medial Geniculate Nucleus of the Guinea Pig During Cardiac Conditioning

Previously we discovered associatively-induced, frequency-specific receptive field

plasticity in auditory cortical fields of the cat (Diamond and Weinberger, 1986) and guinea pig (Bakin, Condon and Weinberger, 1988). During the past year, we have extended this line of inquiry to the auditory thalamus of the guinea pig. This is essential in order to understand the principles of adaptive information processing. At this time, we report on the dorsal division of the medial geniculate nucleus, for which no prior learning data have ever been reported.

Single unit and cluster discharges were recorded in adult guinea pigs before, during and after Pavlovian training (CS=tone, 6.0 sec.; UCS=250 ms footshock at CS offset). Cardiac decelerative conditioned responses developed in all subjects during pairing but not during a prior sensitization period (Figure 4). Frequency receptive fields were determined immediately before and following training by repeatedly presenting a range of tones (50 ms) at different intensities (40-80 db). All acoustic stimuli were delivered with controlled intensity to the contralateral ear. Receptive field plasticity was observed in the majority of both single and cluster recordings (Figures 5, 6).

These findings of receptive field plasticity in the dorsal medial geniculate, which projects to non-primary auditory fields, suggests that interactions between subdivisions of the medial geniculate nucleus and the auditory cortex be studied to understand modifications of information processing during learning. Studies on the ventral and magnocellular division of the MGB are underway. These ongoing experiments are of direct relevance to the model of adaptive information processing in the primary auditory cortex.

Acetylcholine (ACh) Modulation of Auditory Cortical Neurons

Our model of learning-induced receptive plasticity specifies an important role for

cortical ACh. Supported by the USAMDRC and a post-doctoral fellowship to R. Metherate, we have separately shown that ACh can modify receptive fields in auditory cortex in a manner similar to changes induced by learning and that these effects involve muscarinic receptors. (McKenna, Ashe, Hui and Weinberger, 1988; McKenna, Ashe, and Weinberger, in press; Ashe, McKenna and Weinberger, in press; Metherate and Weinberger, 1989). Partial support from this ONR contract has allowed us to obtain cholinergic data relevant to our model of receptive field plasticity.

We have developed a highly specific model of ACh action, as a component of the cortical model, in which this neuromodulator mimics an increase in the sound level of acoustic stimuli (Ashe, McKenna and Weinberger, in press). We present here data that support this model. Furthermore, toward a molecular level of understanding adaptive information processing, we have initiated studies of the role of the muscarinic $M_1$ and $M_2$ sub-types.

In barbiturate-anesthetized guinea pigs, iontophoretically-applied ACh modifies intensity functions (IFs) at best frequency. Responses were increased and thresholds were decreased. Facilitation of evoked responses could decrease IF thresholds by over 10 dB (Figure 7). The effects of ACh thus mimic an increase in stimulus intensity. Since the endogenous release of ACh is increased during increased information processing, this intensity effect may promote attention to and processing of relevant stimuli.

As reviewed above, bc conditioning and ionotophoretic application of ACh to auditory cortex produce shifts in tuning, in which discharges to the CS frequency increase, while responses to other frequencies (including the best frequency)

decrease. These opposite effects suggest that muscarinic receptors may have dual actions. Because muscarinic subtypes have been identified, we sought to determine if these sub-types are involved differentially in increased and decreased responses to tones. We applied the muscarinic receptor antagonists pirenzepine and gallamine to cells whose single tone responses were modified by ACh. Pirenzepine and gallamine are selective antagonists at M1 and M2 muscarinic receptors, respectively. ACh-induced facilitation of spontaneous or evoked activity was antagonized more effectively by pirenzepine than by gallamine (Figures 8, 9). However, gallamine effectively blocked ACh depression of activity (Figure 10). These findings suggest that the modulatory effects of ACh in auditory cortex involve both receptor subtypes, and that different receptor subtypes are involved in "up" and "down" regulation of neuronal discharges.

Response Properties of Single Neurons Within Clusters in Inferior Colliculus and Auditory Cortex: The Need for Single Unit Data During Acquisition

"Cluster" recordings ("multiple unit activity"), consisting of the discharges of several neurons (an indeterminant number) are widely employed, usually because of the great difficulty in recording continually from single neurons in behaving animals (Diamond & Weinberger, 1986). However, the extent to which individual cells within a cluster have the same response characteristics has received little, if any, study. If cells in a cluster have the same characteristics, one could extrapolate cluster data to single neurons. If not, single unit discharges must be sought to enable an understanding of information processing.

In barbiturate-anesthetized guinea pigs, the responses of neuronal clusters to contralateral tone stimulation were obtained using tungsten microelectrodes (tips 1-3 microns, impedances 1-2 megohms). On-line separation of single unit waveforms

was achieved for 2-4 neurons per cluster (central nucleus of inferior colliculus: 16 clusters, 38 cells; primary auditory cortex: 25 clusters, 60 cells) using a computer algorithm that included waveform confidence limits. Response characteristics included best frequency (BF), bandwidth, and discharge pattern. For both the ICc and ACx, differences in one or more characteristics were found in approximately 1/3 to 3/4 of the clusters, including BF differing by at least 0.5 octaves (Table 1 and Figures 11, 12).

These findings indicate that cluster recordings usually consist of the discharges of neurons that have one or more different response characteristics. This limits the interpretation of cluster data and precludes direct extrapolation of such data to single neurons.

Therefore, despite the extreme difficulty of continually recording the discharges of single neurons in the cerebral cortex during behavioral learning, such data appear to be essential to understanding information processing. Accordingly, we have initiated a major effort to achieve this goal. Our approach is to "recover" single unit records from within cluster discharges. During the second year of this contract, our efforts have been greatly assisted by financial support from the Center for the Neurobiology of Learning and Memory, UCI. This has enabled the purchase of a BrainWave Systems computer that is now being programmed to sort waveforms from up to four elctrodes simultaneously.

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Figure 1. Schematic of the Model. Shown are the major components of the model, a greatly abbreviated diagram of the lower auditory system, and their interconnections, not to scale. Abbreviations: ACE, central nucleus of amygdala; CN, cochlear nucleus; IC, inferior colliculus; MGm, magnocellular medial geniculate nucleus; MGv, ventral medial geniculate nucleus; NM, nucleus basalis of Meynart. Roman numerals refer to cortical laminar zones. Grey tone indicates probable site of local plasticity. See text for further details.

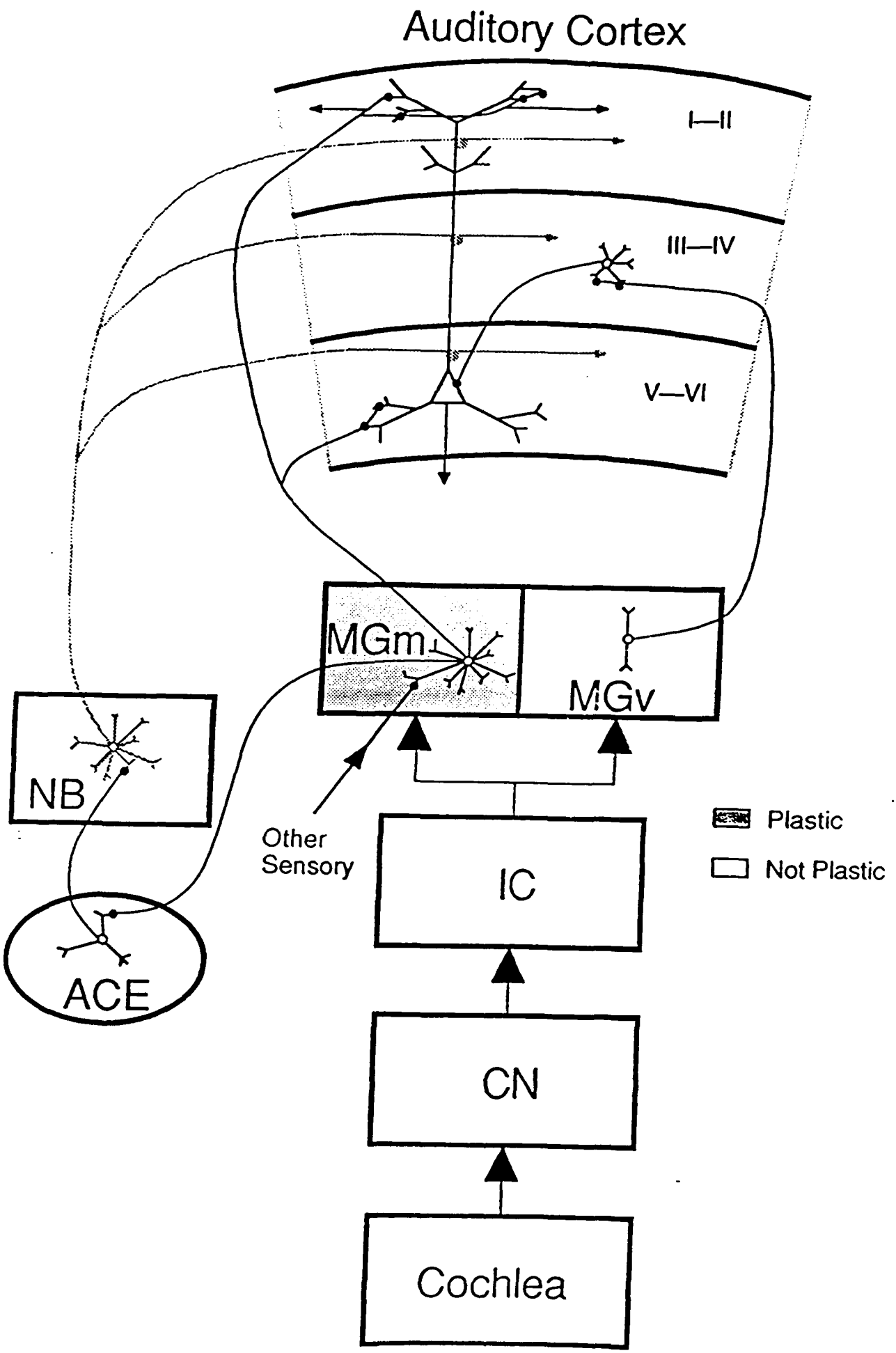
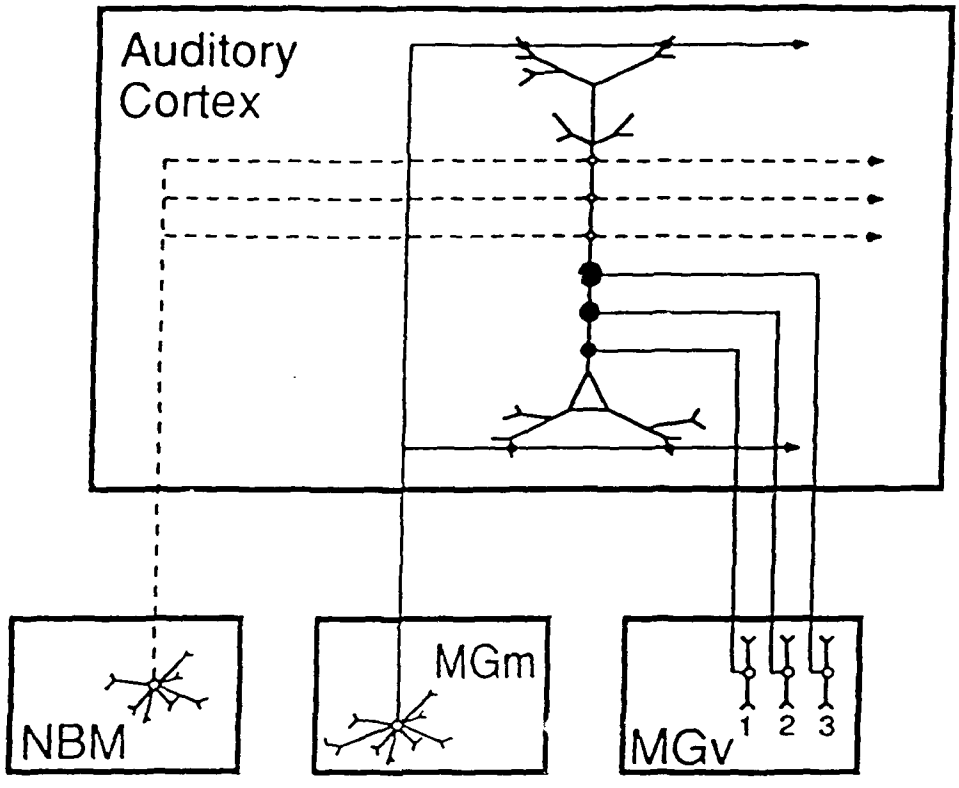

Auditory Cortex
I—II
III—IV
V—VI
MGm
MGv
NB
ACE
Other
Sensory
IC
CN
Cochlea
Plastic
Not Plastic

Figure 2. Schematic Representation of Hypothesized Changes in Synaptic Strengths due to Classical Conditioning. Depicted is a pyramidal cell in primary auditory cortex that receives lemniscal frequency input from the ventral medial geniculate nucleus (MGv); inputs from three frequencies ("1,2,3") that converge on this cell are shown, synapsing on the shaft of the apical dendrite. Also converging on this cell are connections from the magnocellular medial geniculate nucleus (MGm) to the distal apical dendrites in cortical layer I (and also the basilar dendrites), and afferents from the basal nucleus of Meynert (NBM) to the apical dendritic shaft. In this and Figure 3, the synapses from the MGv are represented by filled circles of various sizes, with synaptic strengths proportional to their diameters. The "best frequency" (BF) is that frequency having the greatest synaptic strength for a cell. Top: Pre-conditioning situation, in which the order of synaptic strengths of frequency input is 3>2>1. Bottom: Post-conditioning situation, following classical conditioning in which frequency #2 had been employed as the conditioned stimulus ("CS"). The effects of classical conditioning are shown as if synaptic strengths for the frequency used as the CS were incremented by two arbitrary units (dot diameters) while synaptic strengths to the other frequencies (i.e., #1 and 3) were decreased by one unit. Post-conditioning, the order of synaptic strengths has changed to 2>3>1. Note that the best frequency of this cell was altered from frequency #3 to frequency #2. These changes would produce receptive field plasticity due to learning as previously reported, increased response to the CS frequency and decreased responses to adjacent frequencies.

Pre-Conditioning




Post-Conditioning

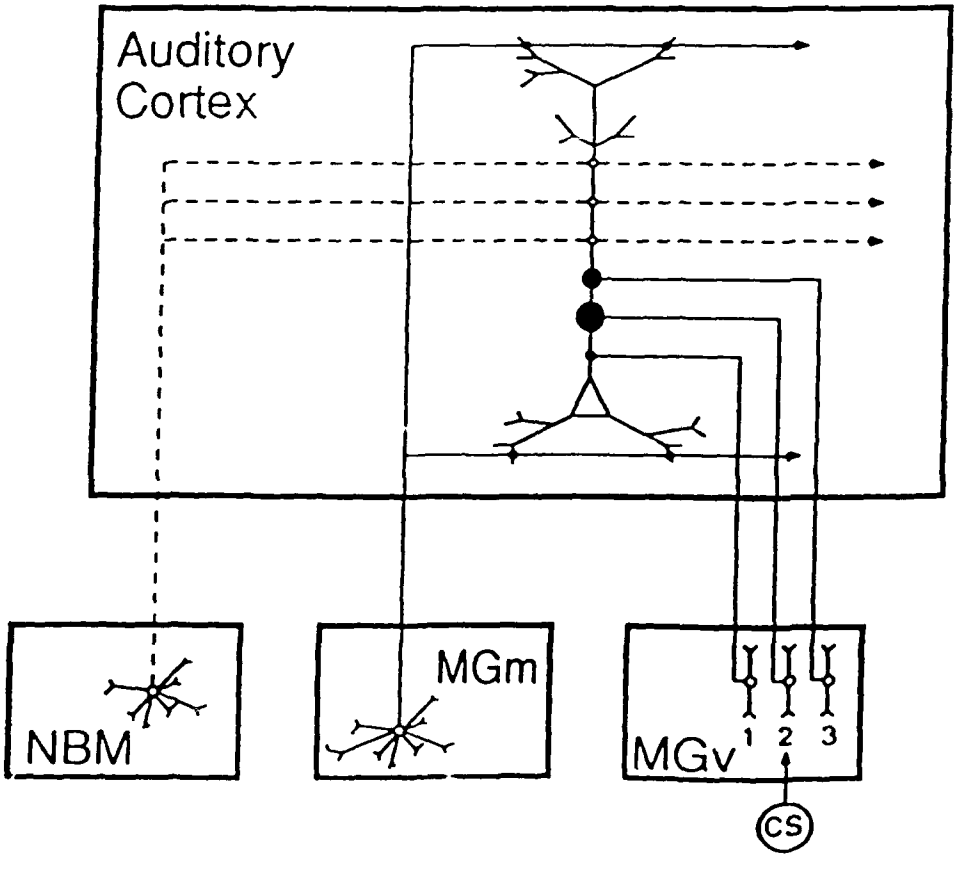
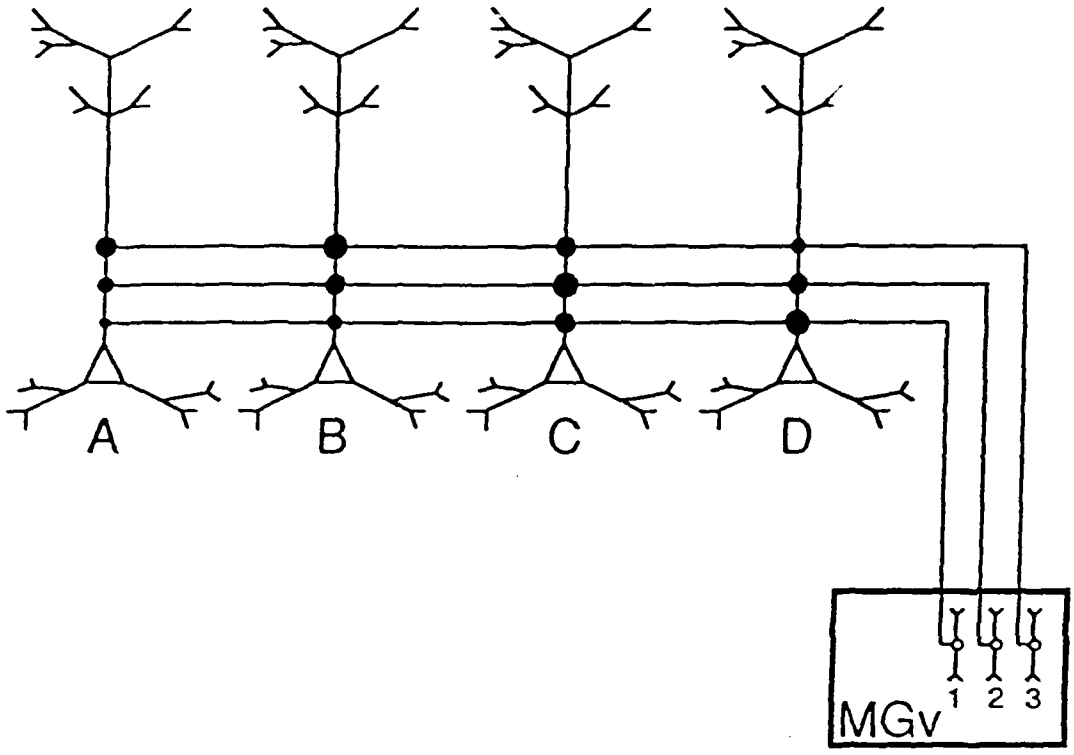
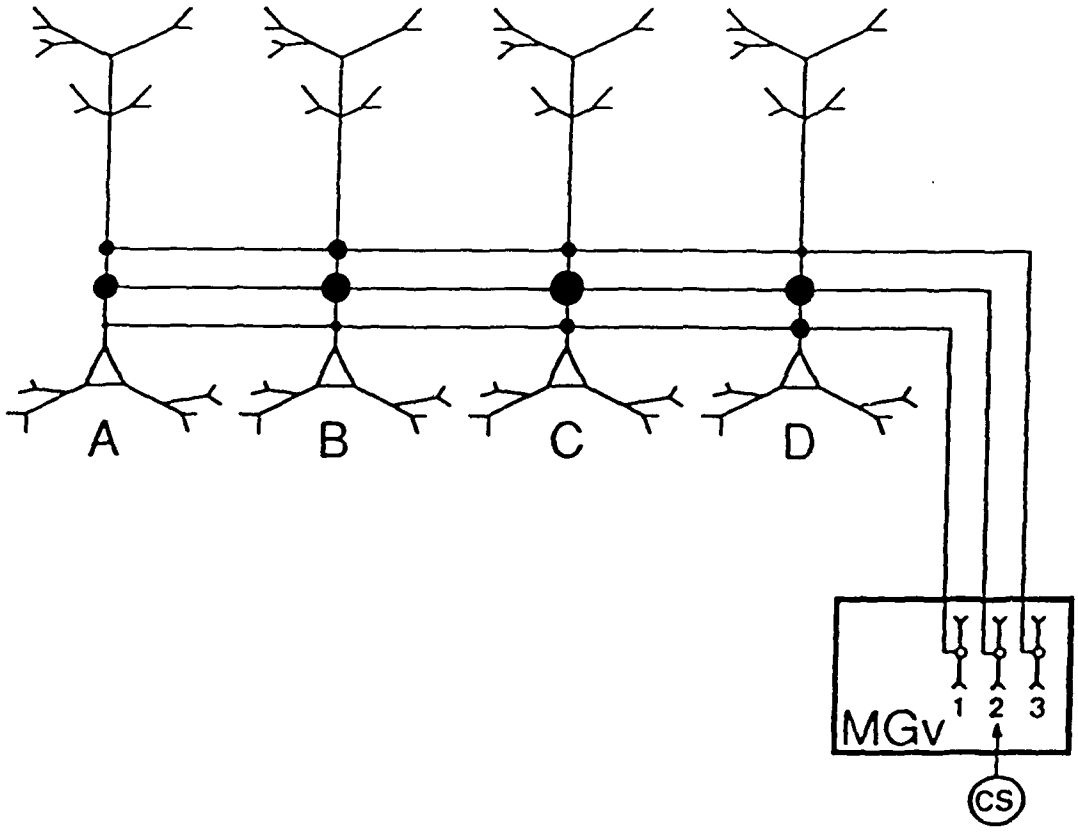


Figure 3. Hypothesized Changes in Synaptic Strengths for Several Neurons Across the Frequency Representation in Primary Auditory Cortex. A schematic drawing of predicted changes (see text) is presented for a subset of auditory cortical neurons. Presented are four neurons and the synaptic strengths of inputs from the ventral medial geniculate nucleus for three different frequencies ("1,2,3"). Top: Pre-Conditioning, the best frequencies for the cells are as follows: A=3, B=3, C=2, D=1. Note the variable strengths of the synapses for the best frequencies, e.g., cells A and B have BF = #3, but responses to this frequency for cell B should be greater than for cell A, similar to common observations in actual experiments. Bottom: Post-Conditioning, following training in which the conditioned stimulus was frequency #2. Synaptic strengths of all inputs have been incremented by two units for frequency #2 and decremented by one unit for frequencies #1 and #3. This has resulted in a shift in best frequency for cells A, B and D to the CS frequency (#2). For cell C, in which the pre-conditioning best frequency was #2, there has been no shift but rather an increased response to this frequency compared to decreased responses to the "side band" frequencies; this situation has not yet been tested in experiments.

Pre-Conditioning




Post-Conditioning



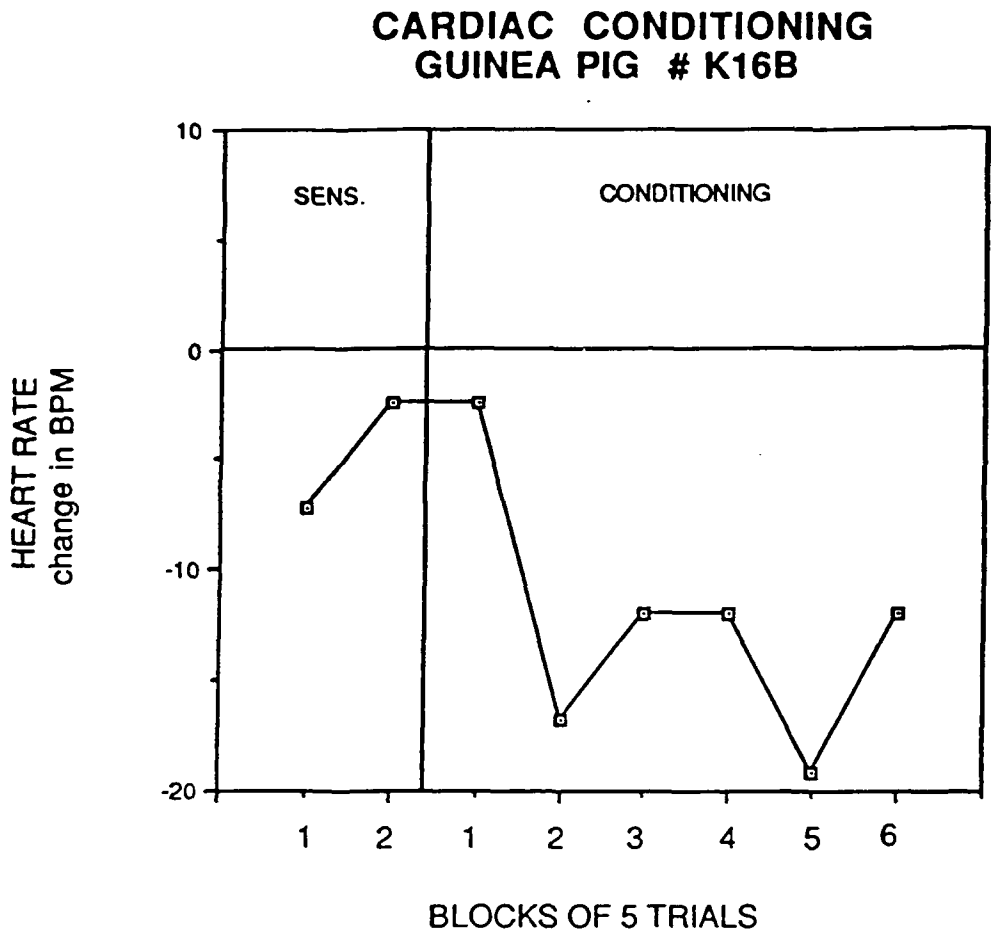
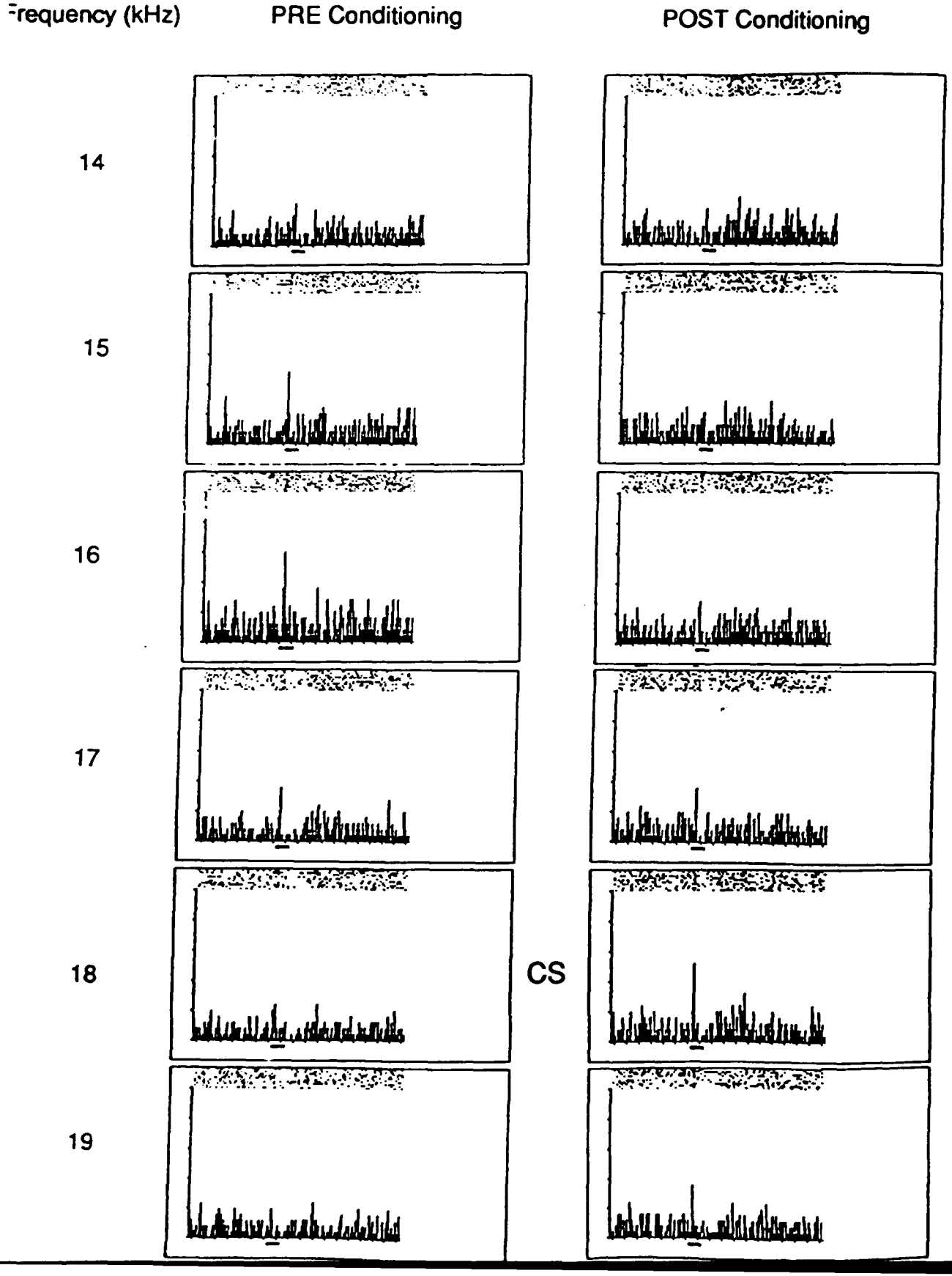



Figure 4. Cardiac Conditioning in the Guinea Pig. Heart rate changes (beats per minute) are shown for the subject (K16B) whose neuronal data are presented in figures 5 and 6. During random presentation of tone and shock during the sensitization control ("SENS"), initial deceleration to tone showed habituation during by the second block of 5 trials. A very large decelerative conditioned response developed by the second block of trials during pairing ("CONDITIONING"). The CS was 18.0 kHz (6.0 sec., 60 db). Note the rapid rate of development of the conditioned response.

Figure 5. Poststimulus Time Histograms for the Receptive Field. PSTH obtained before and after cardiac conditioning in which the conditioned stimulus was 18.0 kHz, for animal K16B. The recordings were obtained from the dorsal division of the medial geniculate nucleus. Note that PRE conditioning, the best frequency (BF) was 16.0 kHz. Following the development of the conditioned response, the BF shifted to 18.0 kHz, the frequency of the conditioned stimulus. Each PSTH is the sum of discharges during 10 stimulus presentations. Stimulus intensity was 60 db. Stimulus duration was 50 ms (bar beneath PSTH) and the vertical axis is 5 spikes per division. Rasters above each PSTH show that the responses were consistent rather than due to large responses on a few presentations.

# NEURONAL DISCHARGES DURING RECEPTIVE FIELD DETERMINATION (# K16B)



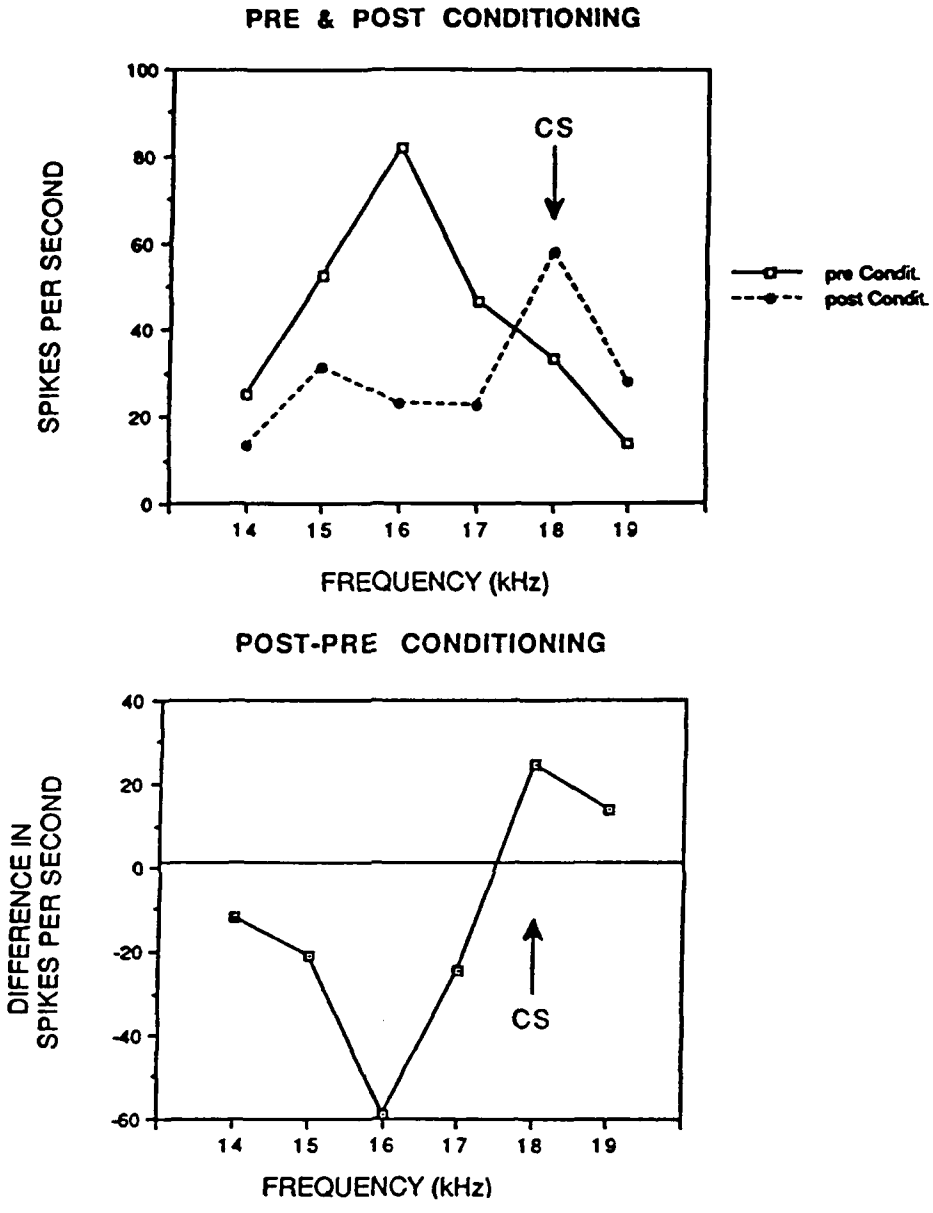



Figure 6. Quantified Receptive Fields for Conditioning. Mean number of spikes per second above spontaneous activity for peak responses during determination of frequency receptive field (see PSTH in Figure 5). The top panel shows the RF before and following conditioning. Note the shift of BF to 18.0 kHz, the CS frequency during intervening conditioning. The bottom panel shows the effect of conditioning, i.e., post minus pre-conditioing tuning. Note that associative conditioning at 18.0 kHz resulted in an increased response at 18.0 and also 19.0 kHz whith a concommitant decreased response to lower frequencies; the largest decrease was at 16.0 kHz, the original best frequency.

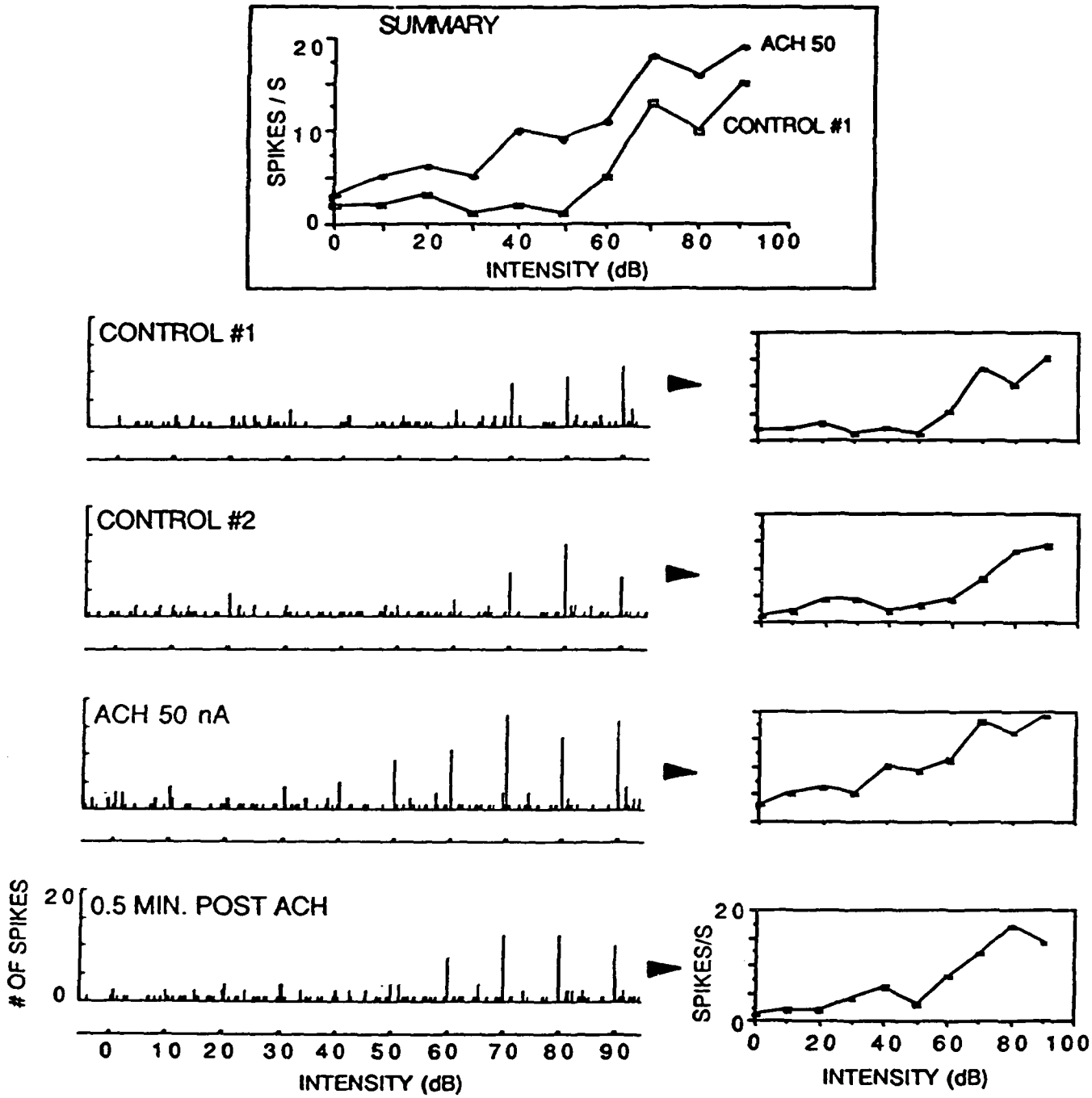



Figure 7. ACh Mimics Increased Acoustic Intensity. Iontophoretic application of ACh increases response magnitude and decreases response threshold. The effect of ACh on a cell's intensity function (IF) is summarized at the top of the figure, and the detailed sequence of events is shown below. On the left are histograms showing the cell's response to the stimulation set (20 trials, each comprised of ten 50 ms tone bursts ranging from 0 to 90 dB SPL at the BF of 1 kHz. Stimulation rate 1/s, bin width 10 ms). The graphs on the right depict the mean discharge during the 50 ms tone duration at each intensity. The cell initially responded strongly to stimuli ranging from 70-90 dB (control #1 and #2). ACh (50 nA) increased the response to these stimuli; as well, the cell responded to stimuli as weak as 10 dB. Near-complete recovery was seen during the stimulation set begun 0.5 min after ACh. Data from primary auditory cortex of barbiturate anesthetized guinea pig.

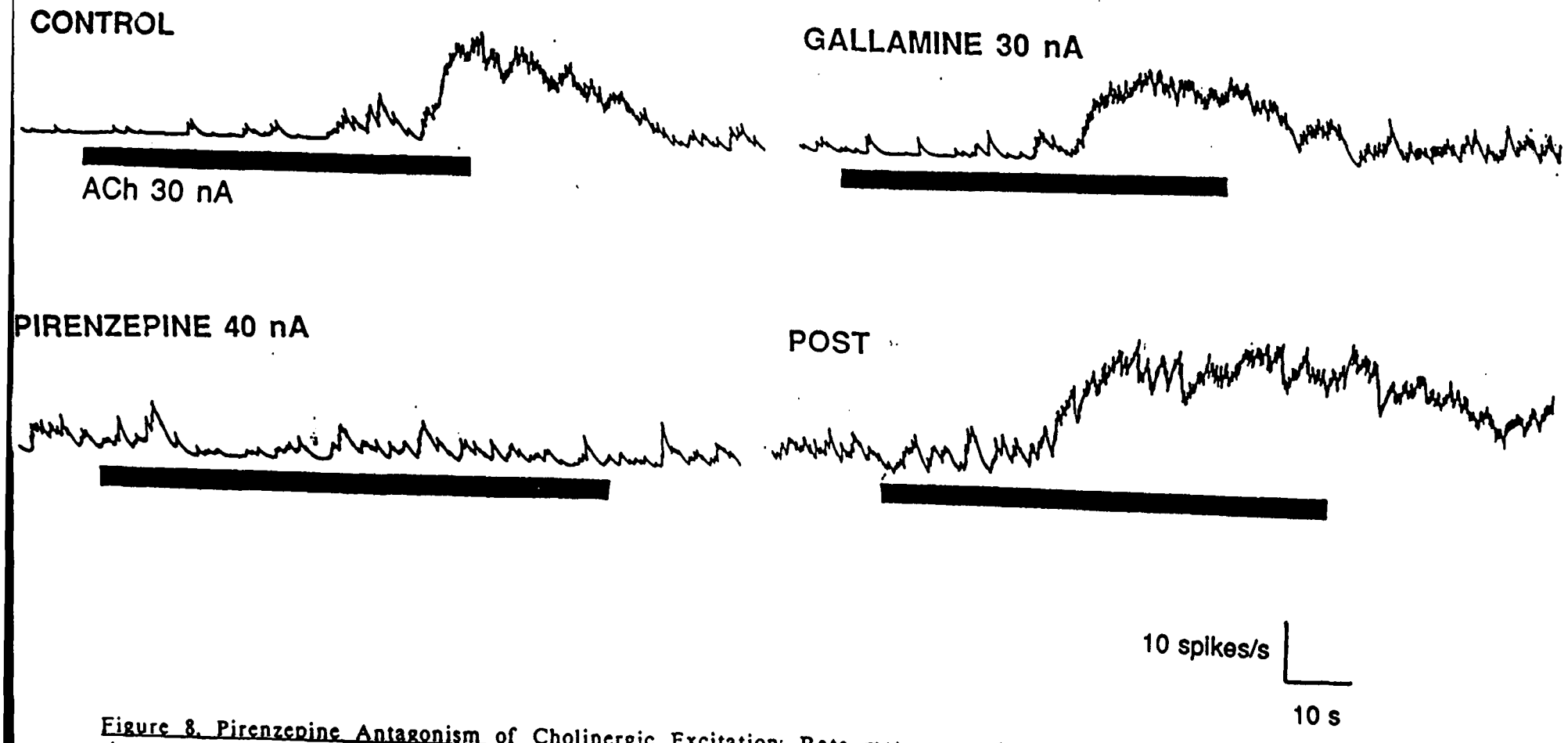



Figure 8. Pirenzepine Antagonism of Cholinergic Excitation: Rate meter records show cholingergic effects on firing rate of a single neuron in primary auditory cortex of the guinea pig. In the control case (top left) ACh strongly facilitated neuronal discharge with its characteristic long latency. The administration of the M2-selective antagonist gallamine did not antagonize the effect of ACh (top right). However, the M1-selective antagonist pirenzepine effectively blocked the cholinergic facilitation (bottom left). This antagonism was transient, and within five minutes the strong facilitation by ACh was seen again (bottom right).

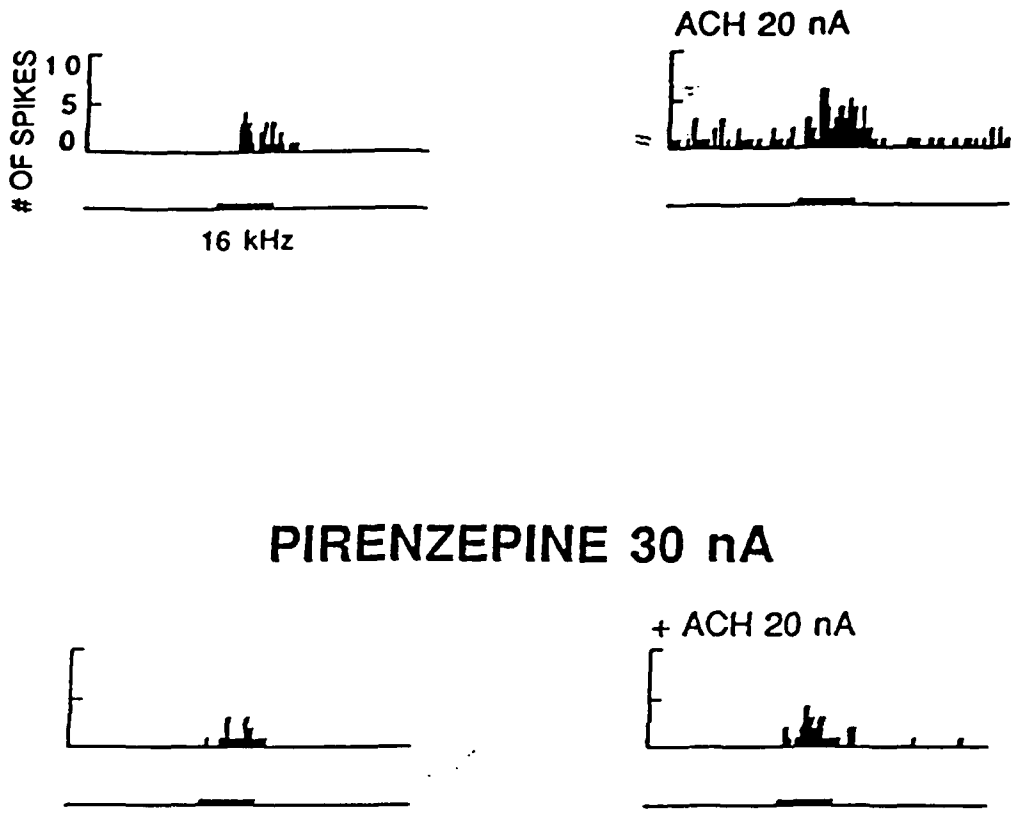



Figure 9. Pirenzepine Antagonizes ACh Facilitation of Evoked Discharges: Records of a cell, in the auditory cortex of the guinea pig, whose best frequency was 16 kHz. The control response to the best frequency tone is shown at top left. ACh (20 nA) facilitated the evoked response and produced spontaneous activity (top right). Administration of pirenzepine alone (30 nA) slightly attenuated the response (bottom left), but effectively blocked the appearance of spontaneous activity and partly antagonized the facilitation of the evoked response (bottom right).

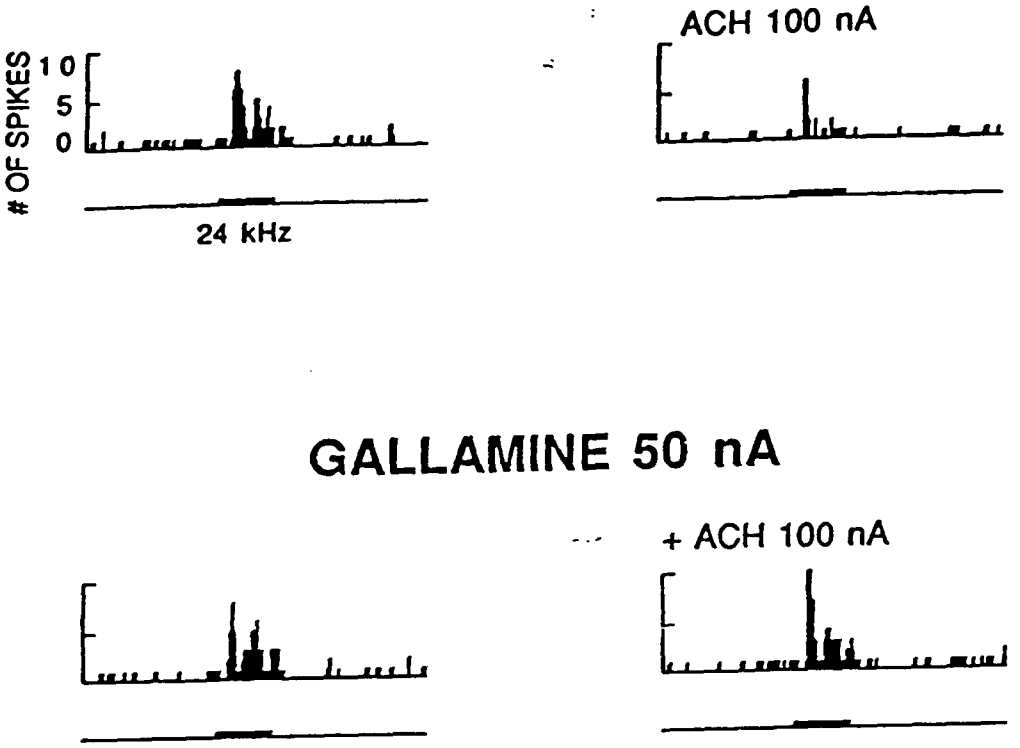
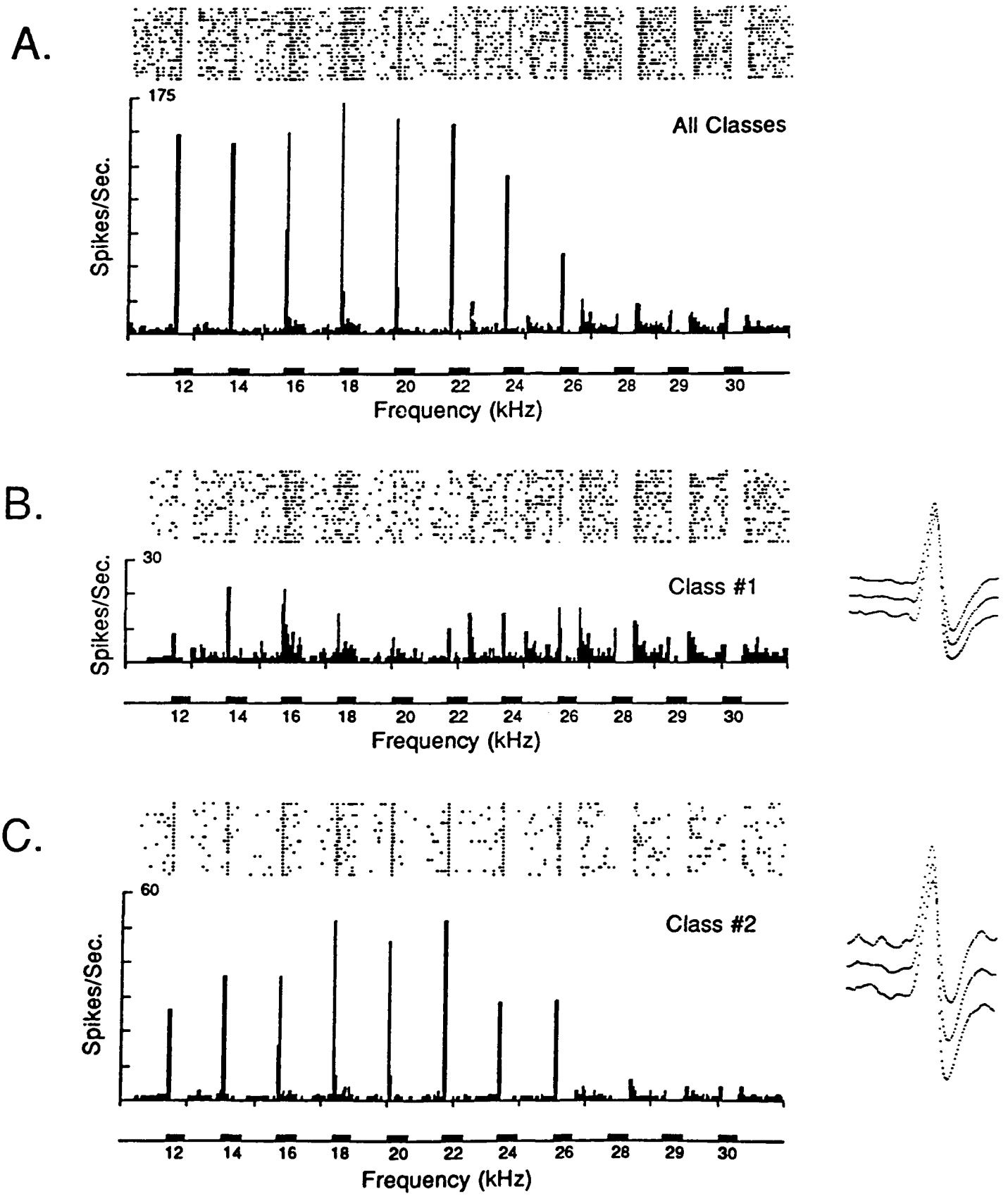



Figure 10. Gallamine Antagonizes ACh Suppression of Evoked Discharges: Records of a cell located in the auditory cortex of guinea pig. It had a best frequency of 24 kHz. Control response to a 80 dB, 24 kHz tone (top left) is strongly suppressed by ACh (100 nA; top right). Gallamine (50 nA) did not by itself alter the evoked response (bottom left), but it effectively antagonized the suppressive effect of ACh.

Figure 11. Separation of Single Units from Cluster Discharges. Poststimulus time histograms for (A) a cluster which responded to stimuli between 12.0 and 30.0 kHz (70 db) and for two neurons (B and C) whose waveforms were sorted from cluster waveforms. Note that the response pattern of the cluster is comprised of two very different patterns: an onset response (12.0 - 26.0 kHz) and a sustained suppression (28.0 - 30.0 kHz). However, the two cells isolated from this cluster contributed both greatly different amounts and somewhat different patterns to the cluster. Waveforms for the single neurons are shown one standard deviation.


A.
175
All Classes
Spikes/Sec.
12 14 16 18 20 22 24 26 28 29 30
Frequency (kHz)
B.
30
Class #1
Spikes/Sec.
12 14 16 18 20 22 24 26 28 29 30
Frequency (kHz)
C.
60
Class #2
Spikes/Sec.
12 14 16 18 20 22 24 26 28 29 30
Frequency (kHz)

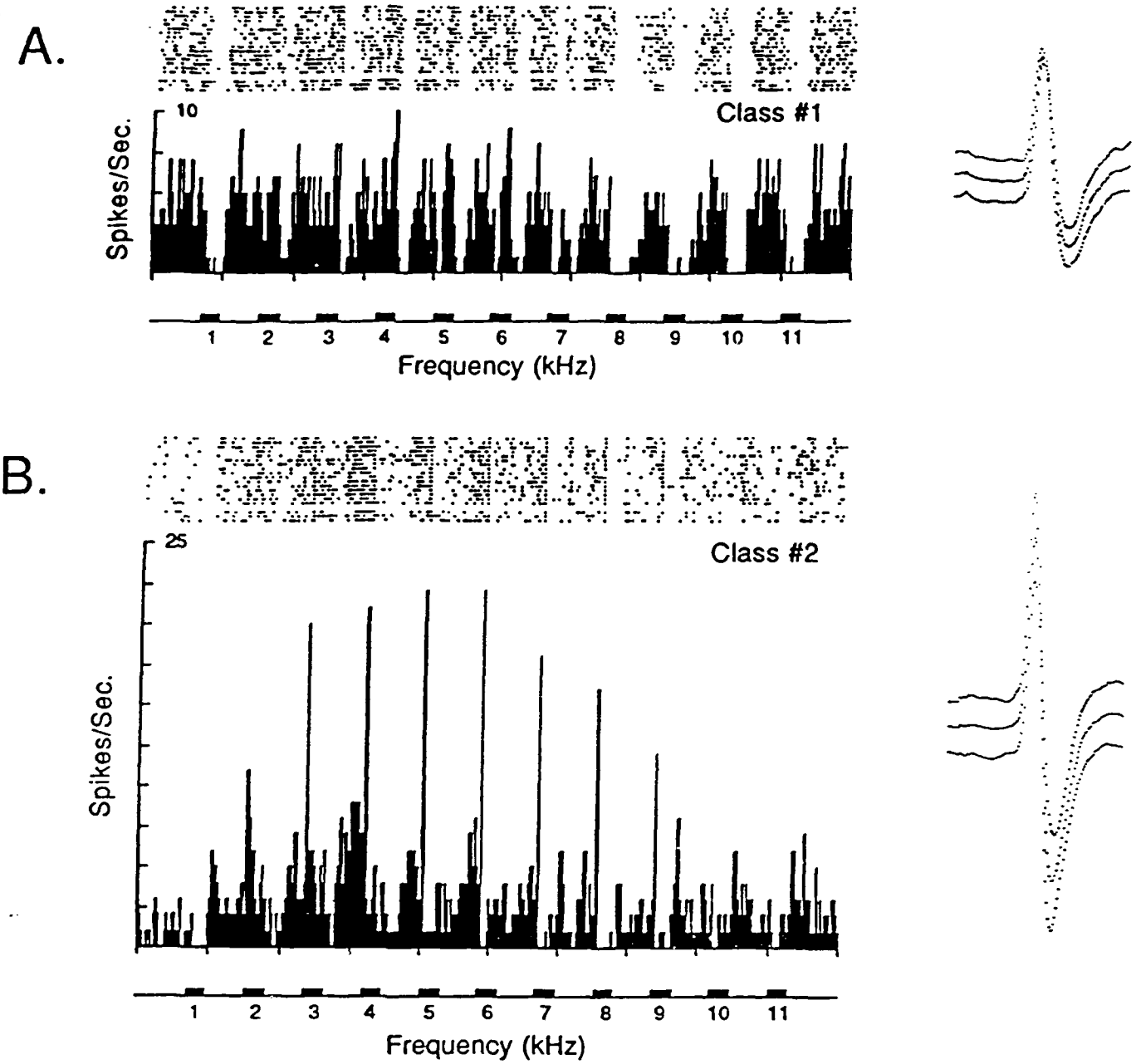



Figure 12. Different Discharge Characteristics of Single Neurons within a Cluster Two neurons isolated from a cluster showing different response patterns, amount of discharges and tuning characteristics. A: This cell had a high rate of background activity and strong suppression during tone with rebound excitation. B: This cell showed some response suppression (e.g., 1 and 8 kHz), but strong onset responses with restricted frequency response.

Table 1. Summary of Discharge Characteristics for Single Neurons Within 16 Clusters All clusters contained neurons with at least one different characteristic and 11/16 clusters had cells that differed in all characterisitics measured. "Resp": magnitude of response. "FRF": frequency receptive field, indexed by best frequency and range of frequency response; "PSTH": pattern of response.

## Table 1— Characteristics of Neurons

| Cluster ID | # of Waveforms | Waveform # | FRF | | PSTH | Resp. | FRF | PSTH |
|---|---|---|---|---|---|---|---|---|
| | | | BF | Range | | | | |
| H14ab1 | 2 | 1 | 14&16 | 12—29 | ON/T/TS | D | D | D |
| | | 2 | 18 | 12—26 | ON/TS | | | |
| H14ad1 | 2 | 1 | 18 | 16—20 | ON/TS | D | S | S |
| | | 2 | 20 | 16—20 | ON/TS | | | |
| H14ba1 | 2 | 1 | 13 | 12—15 | ON/T | D | D | D |
| | | 2 | 7 | 7—8 | ON | | | |
| H14bc1 | 3 | 1 | 24 | 24—30 | ON/TS | D | D | D |
| | | 2 | 28 | 24—30 | T | | | |
| | | 3 | 26 | 24—30 | T | | | |
| H16aa1 | 2 | 1 | 4 | 1—4 | ON | S | D | S |
| | | 2 | 6 | 2—6 | ON | | | |
| H16ab1 | 2 | 1 | 6 | 1—8 | ON/T | D | D | S |
| | | 2 | 5 | 1—10 | ON/T | | | |
| H16ac1 | 2 | 1 | 4 | 4—6 | T/TS | D | D | D |
| | | 2 | 6 | 2—9 | ON/TS | | | |
| H16ad2 | 3 | 1 | 8 | 4—10 | ON | D | D | D |
| | | 2 | 8 | 4—12 | ON/T | | | |
| | | 3 | 8 | 6—8 | ON/T | | | |
| H16ae2 | 3 | 1 | 12 | 10—12 | ON/T | D | D | D |
| | | 2 | 12 | 6—20 | T/TS | | | |
| | | 3 | 10 | 8—18 | ON/T | | | |
| H18aa1 | 2 | 1 | 6 | 1—14 | ON/T | D | D | D |
| | | 2 | 6 | 2—8 | ON | | | |
| H18ab2 | 4 | 1 | 2 | 2—10 | ON/TS/OFF | D | D | D |
| | | 2 | 8 | 1—20 | ON/OFF | | | |
| | | 3 | 4 | 2—12 | ON | | | |
| | | 4 | 8 | 2—18 | ON | | | |
| H18ac2 | 2 | 1 | 4 | 1—10 | ON/T | D | D | D |
| | | 2 | 1 | 1—4 | ON/TS/OFF | | | |
| H18ac4 | 2 | 1 | 22 | 14—30 | T | D | D | D |
| | | 2 | 29 | 22—30 | ON/T | | | |
| H18ad1 | 2 | 1 | 8 | 8—12 | T | S | D | D |
| | | 2 | 8 | 2—12 | ON/TS | | | |
| H18ae1 | 3 | 1 | 8 | 8—18 | ON | D | D | S |
| | | 2 | 8 | 8—18 | ON | | | |
| | | 3 | 12 | 8—18 | ON | | | |
| H18ag1 | 2 | 1 | ? | 6—12 | TS | D | D | D |
| | | 2 | 14 | 10—16 | ON/TS | | | |

S = Same
D = Different

ON = Onset response
T = Through response during tone
TS = Suppression of response during tone
OFF = Response to tone offset

## SUPPORTED BY THIS CONTRACT

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# APPENDIX A

## A MATHEMATICAL MODEL OF ADAPTIVE INFORMATION PROCESSING IN NEOCORTEX

Introduction. We present here a mathematical model of adaptive information processing in the auditory cortex during classical conditioning. We will exploit our extensive experience in creating and analyzing models of learning in trainable machines. Several of these models are described in Pattern Classifiers and Trainable Machines [7]. In particular, we will apply a modification of the window training algorithm devised and validated by Sklansky and Wassel [7].

We will attempt to incorporate known properties of auditory cortical neurons that are related to their adaptive behavior, and to reflect in these models relevant aspects of neuronal interactions, e.g., functional "competition" [2] in sensory neocortex. First we present basic nomenclature.

Nomenclature. The spectral response SR (i.e., "tuning curve" or "frequency receptive field") of an auditory neuron is summarized by a function of output (spikes/second) vs. frequency of a pure sinusoidal tone for isointensity stimuli. (The response area of a neuron includes SR for all effective intensities; for purposes of this project, we will begin by modeling SRs that have been previously obtained at suprathreshold intensities that support behavioral conditioning.) The SR has a peak value at the neuron's peak frequency p. In the absence of conditioning, p is referred to as the neuron's "natural" or "best"

frequency b.

The main training protocol of interest is classical defensive conditioning, in which animals learn to anticipate a mildly noxious stimulus by presenting a sinuoidal tone followed by a weak electrocutaneous stimulus. We refer to this tone in the training protocol as the conditioned stimulus, CS and to all other tones as non-conditioned stimuli, NCS. We refer to the frequencies of the tones in CS and NCS as $\hat{\xi}$ and $\xi$, respectively.

Conditioning Properties. The properties of auditory cortical neurons listed here are based upon previous empirical studies.

1. Conditioning tends to strengthen and broaden the SR curve.
2. During conditioning the p's of auditory cortical neurons shift toward $\hat{\xi}$ unless $b = \hat{\xi}$, in which case response to p increases.
3. If $b = \hat{\xi}$, then the SR of the neuron is symmetric with respect to b. If $b \neq \hat{\xi}$, then SR of the conditioned neuron becomes asymmetric, dragging its tail in moving p toward $\hat{\xi}$.
4. A sequence of NCSs at frequency $\xi$ decreases the amplitude of response of an auditory cortical neuron to an NCS at $\xi$.

Window Training And Gradient Descent. We will use a class of models of machine learning, gradient descent, for modeling learning processes in auditory cortical neural networks. By gradient descent we refer to a broad class of Markovian optimization processes, such as hill climbing and stochastic approximation. A wide range of training procedures for trainable machines can be represented and analyzed by this approach [1,5,6,7,8,9]. In the theory of machine learning, CS training is exemplified by the window training procedure

which was invented, described and tested successfully by Sklansy and Wassel [4,8]. Window training has been shown to have the advantage of better asymptotic performance with respect to error-correcting procedures, both in theory and in practice [7].

In Markovian models of neural learning, the adaptive behavior of a neural network is represented by the motion of a state in state space. We will use Markovian optimization models of learning in the auditory cortex in which the state is a vector whose components determine the current performance of the network. These components may be the set of synaptic connections among the neurons or, more effectively, they may be a relatively small set of mathematical parameters that determine the SRs of the cortical neurons (see below). Let $\underline{r}$ denote a vector whose components are this small set of parameters. (Hence, we refer to $\underline{r}$ as a dimension-reduced vector.) The motion of the state $\underline{r}$ may be either deterministic or stochastic. The performance is a combination of the maximum of the strengths of the responses to the CS after training and the ability of the network to distinguish $\xi$ from other frequencies.

One approach to reducing the dimensionality of state space is through the use of "discriminant functions" [7]. Let $(\xi_i)$ denote a large set of auditory frequencies. For example suppose $\xi_1$=50 Hz, $\xi_2$=51 Hz, $\xi_3$=52 Hz, ..., $\xi_m$=30000 Hz, where m=29951. Construct 100 "discriminant functions", each covering a band of frequencies. Thus each discriminant function is a function of a finite set of adjacent $\xi_i$'s. Denote the outputs of these discriminant functions by $r_1, \ldots r_{100}$. Thus $\underline{r}= (r_1, \ldots, r_{100})^T$ is a dimension-reduced vector that determines the performance of the machine. The training process adjusts just a few of the parameters of each discriminant function rather than the parameters

representing all of the synapses between the pure tone stimulus $\xi$ and the responses of all the auditory cortical neurons. This is a major advantage, because it provides an appropriate level of complexity for modeling the tuning functions of single neurons; consideration of individual synapses would be too detailed and consideration of columns or cell assemblies would be at too gross a level. We may represent the learning process within the auditory cortex in response to n CS's as a trajectory of $\underline{r}(n)$ in state space from an initial state $\underline{r}_A$ to a final state $\underline{r}_B$, as illustrated in Figure 1. In some situations this trajectory represents the mean of a stochastic motion.

The effectiveness of learning upon the frequency tuning of cortical cells may be viewed as a learning-induced change in "performance". Through an analysis based on gradient descent of a performance index $J(\underline{r})$, one may obtain a Markovian differential equation for the mean and variance of the motion of $\underline{r}(n)$. This equation has the following recursive form:

$$\underline{r}(n+1) = \underline{r}(n) + \rho(n)\, \nabla J(\underline{r}), \qquad (1)$$

where $\nabla J(\underline{r})$ is the gradient of $J(\underline{r})$, and $\rho(n)$ is the $n^{th}$ "step size". The choice of step size is related to the speed of convergence and stability [1,5,6].

The solutions to differential equations of this type can answer questions such as the following:

1. Is the trajectory asymptotically stable in the large -- i.e., is its asymptotic behavior independent of the initial position $\underline{r}$? [5]
2. What is the asymptotic variance of $\underline{r}(n)$? [6]
3. What is the likely size of the variance along the path from $\underline{r}_A$ to $\underline{r}_B$ [1]?

4. What determines the speed of convergence to $\underline{r}_B$? Is this speed related to the variance of $\underline{r}(n)$?

Below we combine the concept of multiple discriminant functions with the concept of "competing windows" to formulate a model that accounts for effects of neuronal interaction in auditory cortex during classical conditioning. Because it is a form of window training, this model is subject to analysis by gradient descent and Markovian differential equations [1,5,7,8]. We refer to it as the competing window model.

The "Competing Window" Model

Consider two sets of processors: one set is nonplastic and the other set is plastic. (Here we use "processor" in the sense of an abstract transformer of information.) The nonplastic set represents neurons residing in the ventral medial geniculate nucleus (MGv). The plastic set represents neurons in the auditory cortex, e.g., pyramidal cells. Each nonplastic processor resonates to a narrow band of frequencies, of width $2\delta$ centered about $\xi$, i.e., the interval in x bounded by $\xi \pm \delta$. Thus we refer to each nonplastic processor as a resonator. (These are not to be confused with "adaptive resonance" [3] which is considered a property of the dynamics of learning.) Each plastic processor $C_i$ multiplies and integrates (or sums) the responses of all of the resonators with a window function $A_i\phi_i(x)$ covering a band of frequencies $B_i$. Each $\phi_i(x)$ is nonnegative and is normalized in the sense that its integral over all x is 1. We refer to $A_i$ as the amplitude of the window function. We refer to each plastic processor as a collector. We refer to $\phi_i(x)$ as a normalized window function. The set of $B_i$'s covers the full range of auditory frequencies between 50 Hz and 30000 Hz. Adjacent $B_i$'s may be partially overlapping.

The following is our preliminary concept of the mechanisms of conditioning-induced receptive field plasticity in this model. Both the width $L_i$ of each band $B_i$ and the amplitude $A_i$ are increased if $\hat{\xi} \in B_i$. In addition the peak value $P_i$ of $\phi_i(x)$ is shifted toward $\hat{\xi}$ if $b_i \neq \xi$, where $b_i$ is the "best frequency" of collector $C_i$. The amount of increase in $L_i$, $A_i$ and $\phi_i(x)$ is a monotonic function of the number of training trials, up to behavioral asymptote. If $\xi \notin B_i$, then $L_i$ and $A_i$ may be reduced. The collector $C_i$ that spans $B_i$ represents the average behavior of a group $G_i$ of cortical cells that are physically close to each other. The memberships of the $G_i$'s of cortical cells remain fixed at all times, including the time of the conditioning process. Before conditioning, all of the cortical cells have similarly shaped spectral responses, with peak frequencies uniformally spaced among the cells. After conditioning, the peak frequencies of many cortical cells have shifted toward $\xi$, while dragging the tails of the corresponding SRs. This phenomenon is approximated in our model by replacing all of the cells in $G_i$ by a single collector whose pre-conditioned "best frequency" $b_i$ is the center of $B_i$.

The above phenomena are illustrated in Figure 2. The solid lines show the curves of $\hat{\phi}_i(x)$, which are normalized window functions before conditioning; the dashed lines show $\phi_1(x)$, which is the normalized window function of collector $C_1$ after conditioning. Note that the bandwidth $L_i$ of $\hat{\phi}_1(x)$ is larger than that of $\phi_1(x)$ -- a conjecture that we will test against data. Also shown is the distribution of resonator outputs $v(x,\xi)$ in response to $\xi$.

The response of a collector $C_i$ to a nonconditioned input frequency $\xi$ depends on whether or not $\xi$ lies inside the band $B_i$ spanned by $C_i$. We conjecture that

this response consists of the difference between two sums. The first sum is a component of SR produced by the window function associated with $C_i$; it represents the plastic component that is endogenous to the neuron under observation $[A_i\phi_i(x)]$ multiplied and summed with the frequency response $[v(x,\xi)]$ from the nonplastic MGv to this same neuron. The second sum is the component of SR produced by the window functions associated with $C_j (j \neq i)$ and the window function of $C_i$; this represents the exogenous influence of other cortical cells $C_j$ $(j \neq i)$ on $C_i$. These effects include plastic processes that are attributable to these other neurons $[D_{ij}\phi_i(x)\phi_j(x)]$ and their frequency responses $[v(x,\xi)]$ from the nonplastic MGv. We refer to $D_{ij}$ as the cross-collector amplitude.

Specifically we suggest the following formulation:

$$\text{SR of } C_i = \sum_x A_i \, \phi_i(x) \, v(x,\xi) - \sum_{\substack{j \\ i \neq j}} \sum_x D_{ij} \, \phi_i(x) \, \phi_j(x) \, v(x,\xi). \qquad (2)$$

This equation, if corroborated in analyses, will provide an insight into the competitive nature of learning-induced receptive field plasticity. As discussed previously, conditioning-induced facilitation of response at the CS frequency $\hat{\xi}$ involves decreased responses to lower and higher frequencies, observed as negative "side lobes" (side-band suppression). This effect may be due to a competition among the cortical cells, in which the response of $C_j$ to frequencies in $B_j$ $(j \neq i)$ tends to dominate the response of $C_i$ to $\xi$. Side-band suppression is represented in Eq. (2) by the second, subtractive term. Note that this term produces relatively large negative side lobes in the SRs of $C_1$ and $C_2$ if $B_1$ and $B_2$ overlap sufficiently (Figure 2).

Eq. 2 and Eq. 1 are related in the following way. Eq. 1 determines the trajectory of $\underline{r}(n)$ as a gradient descent on a hill formed by the performance index

$J(\underline{r})$. Eq. 2 establishes constraints which the components of $\underline{r}(n)$ must satisfy for all n. These constraints reflect the competitive nature of cortical interactions. Thus, the performance index $J(\underline{r})$ connects the dynamics of learning in Eq. 1 to the competitive nature of cortical neurons in Eq. 2. $J(\underline{r})$ is of special interest because it may represent an implicit objective in evolution for adaptive information processing in sensory cortex.

In summary, the frequency response (SR) of a cortical neuron is equal to plastic and non-plastic processes that <u>directly</u> affect that cell <u>minus</u> the same types of processes within <u>other</u> cortical cells that <u>indirectly</u> influence the observed neuron (i.e., $C_i$). We believe the above model or a refinement of it will explain conditioning properties described previously.

<u>Specific Aims, Strategy And Procedures</u>

We will refine the competing windows model by <u>simulations based upon neurophysiological data</u> and we will test the model against neuronal data from conditioning experiments.

1. Both B and the amplitude of SR should increase when the number of conditioning trials increases.
2. We expect that the number of cortical cells for which $b = \hat{\xi}$ will increase after conditioning.
3. Negative side bands of $C_i$ and $C_{i+1}$ will increase after conditioning if $b_i < \hat{\xi} < b_{i+1}$. This is a result of the inhibitory effects of the collectors outside of $B_i$.
4. If responses of cells whose b lies outside $B_i$ are decreased (e.g., by habituation or extinction), then the SR of $B_i$ will have reduced negative side lobes.

5. To analyze the learning dynamics of the competing window model we will represent its state by the $A_i$'s and the parameters of the $\phi_i(x)$'s. The motion of this state will be governed by differential equations in accordance with the Sklansky-Merryman theory [6,7].

This motion in state space will be checked against the convergence observed neurophysiologically during previous conditioning experiments.

A distinctive hallmark of the model (see Eq. 2) is that the SR (i.e., frequency receptive field) of a cortical neuron (e.g., pyramidal cell) is determined by two terms (see above): the first includes plasticity that is endogenous to a neuron while the second, subtractive term represents exogenous influences from other cortical neurons. The extent to which cellular neocortical physiological plasticity involves both endogenous and exogenous processes has received little explicit attention in the past.

The competing window model is compatable with our global qualitative model of Rf plasticity (Weinberger et al,10,11) and provides an appropriate mathematical entry point into the global model.